

### **REMARKS**

Claims 287-307 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Glazer et al. (US 5,646,264) in view of Lee et al. (US 5,945,526). The Examiner states the following:

Glazer discloses in Figure 4 the synthesis a heterodimeric dye composition comprising a first dye that comprises a phenanthridinium moiety and a second dye that is different from the first dye. The linker that links both dyes can comprise bromine or chlorine counter-ion.

Glazer does not show that the attachment is through the phenyl ring.

Lee et al. disclose heterodimeric dye where the attachment is through a phenyl ring in ortho, meta or para position. See col. 6, Tables 1-5.

Therefore it would have been obvious at the time the invention was made to synthesis heterodimeric dyes as taught by Glazer comprising an attachment via the phenyl ring as shown by Lee. The motivation is that the attachment is provided on a ring that is less steric and also viewed as an electrophilic moiety and more reactive toward nucleophilic moiety. It is well know in the art of organic chemistry that a phenyl ring comprising an electron withdrawing moiety such as the phenanthridinium moiety will be more reactive toward nucleophilic group and therefore can be substituted in ortho, meta or para position.

Applicants argue that the references do not feature the position of the linkage to the second dye through the phenyl ring of the phenanthridinium moiety. This is not convincing because Lee et al do show such linkage. Additionally applicants mentioned unexpected results. Said unexpected results are discussed in their response filed 1/13/06. However said unexpected results are based on homodimeric compounds (two ethidium bromide molecules joined together

through their phenyl groups), not heterodimeric as claimed.  
There is no disclosure of unexpected results for the heterodimeric dye composition.

The Examiner has not established a prima facie case of obviousness because she has not shown a motivation or suggestion to combine Glazer with Lee. While the Examiner does state reasons why the phenyl ring would be an appropriate site for attachment, she does not provide evidence of any particular motivation to do so. It is not simply a question of whether it is obvious that a practitioner could do something as much as whether a practitioner would have an incentive (or the motivation) to do so. The mere possibility that the dye in the prior art could be modified or replaced (through the use of a phenyl group) such that its use would lead to the dye compositions cited in claims 287-307 does not make the composition cited in claims 287-307 obvious unless the prior art suggests the desirability of such a modification (see MPEP 2144.08 IIA). "The consistent criterion for determination of obviousness is whether the prior art would have suggested to one of ordinary skill in the art that this process should be carried out..." (*Hodosh v. Block Drug Co.*, 786 F.2d 1136, 1143 n.5, 229 USPQ 182, 187 n.5 (Fed. Cir. 1986), cited in MPEP 2144.08 IIA (emphasis added)).

While the Examiner states that the motivation is less steric hindrance and more reactivity, all persons skilled in the art have always been aware of this "motivation", yet not one has ever actually done it. If it was indeed obvious, it would have already been carried out and would be found in the prior art. It has not, and there is no prior art to show otherwise.

There is no expression of any particular problem that is being solved such that the previously described chemistry of attaching moieties to the anthridinium ring should be substituted by what the Examiner has described as "obvious" chemistry. That there was a lack of motivation is abundantly clear from the fact that the di-ethidium molecule was first described in 1983 using the anthridinium portion and there were no reports of a

di-ethidium molecule joined through the phenyl portion when the present application was filed in 2002 (19 years later). The substitution of a different dye for one of the anthridinium moieties was described in a paper by Glazer's group in 1993 (Benson et al., Nucleic Acids Research 21; 5727-5735) before the '264 Glazer patent was issued. At the time of publication, the potential use of the phenyl ring was known in the art of organic chemistry without the need for that which is described in the '526 Lee patent. Thus, there is a 9 year gap between the Glazer publication and the Rabbani filing where no one took what the Examiner considers to be "obvious" steps. Even if the Examiner believes that access to the '526 Lee patent may have increased the incentive to use a phenyl ring between two dyes, the same type of molecules were published in a paper by the inventors of the '526 patent in 1997 (Rosenblum et al., Nucleic Acids Research 25; 4500-4504). And even though this information was made public, for the intervening five years between the publication of the Rosenblum paper and the filing of the present application, nothing surfaced showing the application of this method to joining dyes to ethidium bromide. In summary, although information has been available for how to join a dye to the phenyl ring of anthridinium before the filing of this patent application, there was no obvious need or desire to do so before Applicants' filing.

In contrast to the lack of motivation by others, we have previously discussed with the Examiner our motivation, which stems from the fact that we achieved unexpected results when linking together two ethidium molecules through a phenyl group. While the Examiner is correct in stating that there was no disclosure of unexpected results from a heterodimeric compound through the phenyl group, the unexpected results we obtained from the creation of a homodimeric compound resulted in an appreciation that this could also be applied to a heterodimeric compound. Only applicants had access to the unexpected results – they were not in the prior art. And these same unexpected results provided the motivation to create a heterodimeric dye composition using a phenyl group, which is the present invention. The creation of a heterodimeric dye through the phenyl group remained unobvious to others because they lacked the information about

the unexpected properties of the homodimeric dye, and thus lacked the motivation to form such dyes. In contrast, the present inventors had access to this unique and new information which motivated them to apply this principle to other dye partners.

In conclusion, Applicants disagree with the Examiner's viewpoint on obviousness and stress that the lack of any public record disclosing the joining together of dyes through the phenyl group of ethidium is a strong indication that there has been a lack of motivation to carry out the invention prior to Applicants' discovery of unique properties when a homodimer was made this way.

Stravrianopoulos et al.

Serial No.: 10/764,389

Filed: January 23, 2004

Page 7 Reply To August 17, 2006 Office Action – February 15, 2007

**SUMMARY**

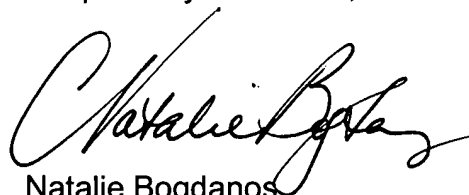
In view of the foregoing remarks, Applicants respectfully request reconsideration and withdrawal of the sole rejection of record of claims 287-307. Therefore, claims 287-307 are presented for further examination.

Early and favorable action is respectfully requested.

No other fee or fees are believed due in connection with this paper. In the event that any fee or fees are due, however, the United States Patent and Trademark Office is hereby authorized to charge any such fee or fees to Deposit Account No. 05-1135, or to credit any overpayment thereto.

If a telephone conversation would further the prosecution of the present application, Applicants' undersigned attorney requests that she be contacted at the number provided below.

Respectfully submitted,

A handwritten signature in black ink, appearing to read "Natalie Bogdanos", with a stylized flourish at the end.

Natalie Bogdanos  
Registration No. 51,480  
Attorney for Applicants

ENZO LIFE SCIENCES, INC.  
c/o ENZO BIOCHEM, INC.  
527 Madison Avenue, 9<sup>th</sup> Floor  
New York, New York 10022-4304  
Telephone: (212) 583-0100  
Facsimile: (212) 583-0150

al/USProsecution/Enz-61(D8).ReplyToOfficeAction.021507

**Enz-61(D8)**